Complete Summary

GUIDELINE TITLE

Androgen therapy in women: an Endocrine Society clinical practice guideline.

BIBLIOGRAPHIC SOURCE(S)

Wierman ME, Basson R, Davis SR, Khosla S, Miller KK, Rosner W, Santoro N. Androgen therapy in women: an Endocrine Society Clinical Practice guideline. J Clin Endocrinol Metab 2006 Oct;91(10):3697-710. [151 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Androgen deficiency

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management

CLINICAL SPECIALTY

Endocrinology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To provide guidelines for the therapeutic use of androgens in women
- To outline the areas of future research

TARGET POPULATION

Women with androgen deficiency

INTERVENTIONS AND PRACTICES CONSIDERED

Androgen therapy

MAJOR OUTCOMES CONSIDERED

- Accuracy (sensitivity, specificity) of existing methods of testosterone measurement
- Response to androgen therapy in terms of bone mineral density, cognitive function, quality of life, sexual function, mood, cardiovascular function, body composition, and muscle strength and function in women with androgen deficiency
- Safety profile of androgen therapy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of the Evidence

+OOO Denotes very low quality evidence

++OO Denotes low quality evidence

+++O Denotes moderate quality evidence

++++ Denotes high quality evidence

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Participants

The Task Force was composed of a chair, selected by the Clinical Guidelines Subcommittee (CGS) of The Endocrine Society, six additional experts, a methodologist, and a medical writer.

Evidence

The Task Force used systematic reviews of available evidence to inform its key recommendations. The Task Force used consistent language and graphical descriptions of both the strength of recommendation and the quality of evidence, using the recommendations of the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system.

Consensus Process

Consensus was guided by systematic reviews of evidence and discussions during one group meeting, several conference calls, and e-mail communications.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendations

- The number 1 indicates a strong recommendation and is associated with the phrase "The Task Force recommends."
- The number 2 denotes a weak recommendation and is associated with the phrase "The Task Force suggests."

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The drafts prepared by the task force with the help of a medical writer were reviewed successively by The Endocrine Society's Clinical Guidelines Subcommittee (CGS), Clinical Affairs Committee (CAC), and Executive Committee. The version approved by the CGS and the CAC was placed on The Endocrine Society's Web site for comments by members. At each stage of review, the Task Force received written comments and incorporated needed changes.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the quality of the evidence (+OOO, ++OO, +++O, and ++++); the strength of the recommendation (1 or 2); and for the difference between a "recommendation" and a "suggestion" are provided at the end of the "Major Recommendations" field.

Diagnosis

The Task Force recommends against making a diagnosis of androgen deficiency in women at this time because there is neither a well-defined clinical syndrome nor normative data on testosterone or free testosterone levels in women across their lifespans that can be used to define the disorder (1 | +OOO).

Treatment

Although evidence exists for short-term efficacy of testosterone in selected populations, such as surgically menopausal women, the Task Force recommends against the generalized use of testosterone by women because the indications are inadequate and evidence of safety in long-term studies is lacking (1 | +OOO).

To formulate clinical recommendations, the task force would require additional data 1) defining conditions that, when not treated with androgens, have adverse health consequences to women; 2) defining clinical and laboratory parameters that distinguish those with these conditions; and 3) assessing the efficacy and long-term safety of androgen administration on outcomes that are important to women diagnosed with these conditions.

This necessary clinical research cannot occur until the biological, physiological, and psychological underpinnings of the role of androgens in women and candidate

disorders are further elucidated. Thus, the task force makes the following recommendations to the clinical and research community.

Needed Assays

The Task Force recommends the development of sensitive and specific assays to measure testosterone and free testosterone in women across their lifespans (1 | +++O).

Needed Research

The Task Force recommends additional research in the following human model systems to define the clinical syndrome of androgen deficiency and to study the benefits and risks of androgen therapy (1 | +OOO):

- Surgical menopause is a condition in which the ovarian, but not adrenal androgen precursors are removed abruptly independent of age.
- Hypopituitarism, although uncommon, can be used to study the physiological replacement of both ovarian androgens and adrenal androgen precursors.
- Anorexia nervosa may be used as a model of androgen deficiency secondary to dysfunction of the hypothalamic-pituitary and adrenal axes.
- Primary adrenal insufficiency allows for the investigation of the loss of adrenal androgen precursors in the presence of intact ovarian androgen function.
- Ablation-replacement models in normal women using GnRH analogs to eliminate ovarian androgens, with or without suppression of adrenal androgen precursors, offer another way to assess the effects of androgen withdrawal and replacement.
- Subjects with complete androgen insensitivity syndrome offer a way to investigate target tissue effects which are dependent on the androgen receptor but are independent of aromatization.
- There are studies in patients with low weight and HIV and with natural aging; however, these systems are too complex to recommend as initial models to understand the potential therapeutic role of androgens in women.

The Task Force recommends additional investigation using rodent and primate models to further define the specific targets of androgen action (1 | +OOO).

The Task Force recommends additional research into the role of local androgen production, action, and metabolism in tissues (1 | +OOO).

The Task Force recommends further study of physiologic targets of androgen action (1 | +OOO) such as:

- Sexual dysfunction
- Cognition
- Mood
- Bone
- Cardiovascular function
- Body composition
- Muscle strength and function

The Task Force recommends the following endpoints be considered for safety and risk assessment in future studies (1 | +OOO):

- Appearance of or change in hirsutism, acne, male pattern balding, clitoromegaly, and deepening of the voice.
- Cardiovascular and metabolic evaluation, with and without estrogen replacement, should include fasting lipid profiles, vascular reactivity, markers of insulin sensitivity, and markers of inflammation.
- Effects on the breast, with or without estrogen replacement, should be measured. Breast biopsy studies with *in vitro* markers of cell proliferation and apoptosis should be considered.
- Alterations in the endometrium with and without estrogen coadministration
- Alterations in mood using validated instruments

Definitions:

Strength of Recommendations

1 - Indicates a strong recommendation and is associated with the phrase "The Task Force recommends."

2 - Denotes a weak recommendation and is associated with the phrase "The Task Force suggests."

Quality of the Evidence

+OOO Denotes very low quality evidence

++OO Denotes low quality evidence

+++O Denotes moderate quality evidence

++++ Denotes high quality evidence

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The quality of the supporting evidence is identified and graded for each recommendation (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Outlining the areas of additional research in human and animal models to allow future recommendations on diagnosis and treatment

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Clinical Practice Guidelines are developed to be of assistance to endocrinologists by providing guidance and recommendations for particular areas of practice. The Guidelines should not be considered inclusive of all proper approaches or methods, or exclusive of others. The Guidelines cannot guarantee any specific outcome, nor do they establish a standard of care. The Guidelines are not intended to dictate the treatment of a particular patient. Treatment decisions must be made based on the independent judgment of health care providers and each patient's individual circumstances.
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IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006

GUIDELINE DEVELOPER(S)

The Endocrine Society - Disease Specific Society

SOURCE(S) OF FUNDING

The Endocrine Society

GUIDELINE COMMITTEE

Androgen Therapy in Women Guideline Task Force

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Task Force Members: Margaret E. Wierman; Rosemary Basson; Susan R. Davis; Sundeep Khosla; Karen K. Miller; William Rosner; Nanette Santoro

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The Task Force received no corporate funding or remuneration.

Margaret E. Wierman, MD (chair)—Consultation or Advisement: None Declared; Grant or Other Research Support: None Declared; Honoraria: None Declared; Speakers Bureau: Merck, Pfizer. Rosemary Basson, MD, FRCP—Consultation or Advisement: Solvay Pharma; Grant or Other Research Support: None Declared; Speakers Bureau: None Declared. Susan R. Davis, MBBS, MD, FRACP, PhD—Consultation or Advisement: P&G, Cellergy, USA; Vivus, USA; Acrux Pty Ltd, Australia; Organon, Netherlands; Research Support: Acrux, Wyeth, AstraZeneca; Honorarium (separate to consultants): Organon, P&G; Other: Institution receives payment for the conduct of industry sponsored research from Organon, P&G. Sundeep Khosla, MD—Consultation or Advisement: None Declared; Grant or Other Research Support: None Declared. Karen K. Miller, MD— Consultation or Advisement: P&G, Auxilium; Grant or Other Research Support: Genentech; Other (study medications only): Genentech, P&G. William Rosner, MD—Consultation or

Advisement: Solvay Pharma; Grant or Other Research Support: None Declared. Nanette F. Santoro, MD—Consultation or Advisement: P&G, TAP, Wyeth, Pfizer, QuantRX; Grant or Other Research Support: Ferring, Novo Nordisk

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from The Endocrine Society Web site.

Print copies: Available from The Endocrine Society, c/o Bank of America, P.O. Box 630721, Baltimore, MD 21263-0736; Phone: (301) 941.0210; Email: Societyservices@endo-society.org

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

The following is available:

- Patient guide to the therapeutic use of androgens in women. Chevy Chase (MD): The Hormone Foundation; 2006 Oct. 2 p.

Electronic copies: Available in Portable Document Format (PDF) from The Hormone Society Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on December 13, 2006. The information was verified by the guideline developer on January 12, 2007.

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